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Epigenetic and signaling mechanisms underlying the reduced response of dendritic cells from aged humans to influenza infections

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Increased susceptibility to respiratory infections is a major cause of age-related morbidity and mortality. Impaired age-associated T and B cell responses are prime suspect yet the mechanisms responsible for the increased risk are complex and are not well understood. Studies in recent years highlight the importance of innate immune cells such as dendritic cells (DC) in fighting infections and generating protective immunity. Our results indicate that monocyte derived DCs from aged subjects display a higher basal level of activation as evidenced by increased activation of NF κ B at the basal level. Moreover, the response of aged DCs to influenza virus is impaired and there is reduced secretion of IFN-I and IFN-III compared to their young counterparts. During viral infections, IFNs are expressed and constitute perhaps the most important line of innate antiviral defense. Type III IFNs act specifically on mucosal epithelia and therefore, play an important role in the defense against infections of the respiratory tract. Our investigations demonstrate that reduced phosphorylation of Interferon Regulatory Factor-7 (IRF-7) in aged DCs may be responsible for the reduced IFN secretion. Furthermore, we found that there may be increased association of IFN-I and IFN-III promoters with suppressor histone, H3K9 in aged DCs. Age-associated alterations in signaling as well as chromatin remodeling may therefore be responsible for the reduced secretion of IFNs by aged DCs and increased susceptibility to influenza infections

Biography

Anshu Agrawal completed Ph.D. from Central Drug Research Institute, Lucknow and subsequently worked as a Research Scientist in the division of immunology at ICGEB, India. She won a scholarship to work in France and after completing postdoctoral studies is now working as a faculty in the Department of Medicine, University of California, Irvine since last 6 years. She is the recipient of the New Scholar award in aging from the Ellison Medical Foundation. She has published more than 30 papers and serves as an editorial board member and reviewer for several journals. Her primary area of interest is dendritic cells, innate immunity and aging.